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10/586,780

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Yong-Chul Kim

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EXAMINER

YOUNG, SHAWQUA

ART UNIT

PAPER NUMBER

1626

MAIL DATE

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12/26/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|-----------------------------------|--|
| Office Action Summary | Application No. 10/586,780 | Applicant(s) KIM ET AL. | |
| | Examiner SHAWQUIA YOUNG | Art Unit 1626 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 October 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) 4,7-10 and 15-18 is/are allowed.
- 6) ☒ Claim(s) 5,6 and 11-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 4-18 are currently pending in the instant application. Applicants have amended claim 4-8 in an amendment filed on October 17, 2008.

I. *Response to Arguments*

Applicant's amendment, filed on October 17, 2008, has overcome the rejection of claims 4-18 under 35 USC 112, second paragraph as being indefinite. The rejection has been withdrawn.

Applicants' arguments has been fully considered but are not found persuasive for the rejection of claims 5, 6 and 11-14 under 35 USC 103 as being unpatentable over Meijer, et al. (US 2007/0276025). Applicants argue that the claimed compounds in claim 5 and 6 have fluorine and chlorine, respectively at the 5-position while the 7-position is unsubstituted. Applicants further argue that none of the compounds in the prior art reference teaches a fluorine or chlorine at the 5-position with the 7-position unsubstituted. Applicants cite an example from the specification in support of their arguments. The example is between the compound of claim 6 and another compound (AGM0017) whereas the compound differs from the claimed compound because it has a methyl group at the 7-position. This addition of a methyl group at the 7-position does not have an inhibitory effect on cancer cell proliferation.

However, the Examiner wants to point out that in Figure 1 of the prior art reference, there is a table with various species including a 6-bromoindirubin-3'-oxime (See compound 7a in the table). In paragraph 0017 on page 2, the prior art references

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teaches that the indirubin-3'-oxime can be substituted with a halogen at the 6-position. So it teaches other halogens (i.e., Cl, F, etc.) and the only difference between the above species and the instant claimed compounds is the position of the halogen atom. Applicants have failed to show the effects of moving the halogen atom from the 5-position to other positions on the phenyl ring (i.e. 6-position) by disclosing comparison data. The prior art also teaches in table 5 on page 27 a variety of compounds including 6-chloroindirubin-3'-oxime and 5,6-dichloroindirubin-3'-oxime and the references further teaches that in previous studies it had been demonstrated that the indirubin derivatives substituted on position 5 exhibited an enhanced inhibitory activity (See paragraph 0213, page 21). This teaching support the motivation for taking the compounds disclosed in the prior art and preparing similar compounds wherein the halogen atoms are substituted on the 5-position. Thus, the Examiner has maintained the rejection.

II. *Rejections*

35 USC § 103 - OBVIOUSNESS REJECTION

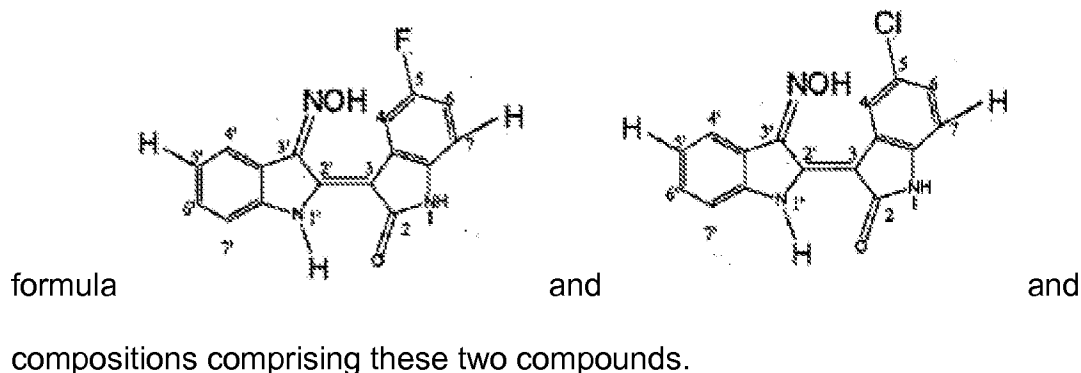
The following is a quotation of 35 U.S.C. § 103(a) that forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Graham v. John Deere Co. set forth the factual inquiries necessary to determine obviousness under 35 U.S.C. §103(a). See *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Specifically, the analysis must employ the following factual inquiries:

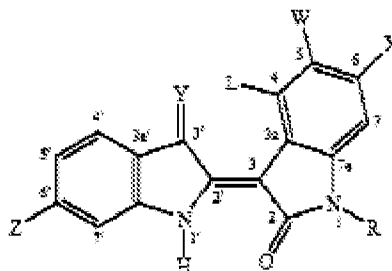
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 5, 6 and 11-14 are rejected under 35 U.S.C. § 103(a) as being unpatentable over *Meijer, et al.* (US 2007/0276025). Applicants claim compounds of



The Scope and Content of the Prior Art (MPEP §2141.01)

Meijer, et al. teaches indirubin-type compound that are modulators of glycogen synthase kinase-3, cyclin-dependent protein kinases or aryl hydrocarbon receptors. The



invention is represented by the general formula:

wherein X represents Br, Cl, I, F, CH=CH₂, or H; Y represents NOH, NOAc, NOCH₃ or O; Z represents H; W represents H, CH₃, Cl or NO₂; L represents H or Cl; R represents H or CH₃ (See page 27, table 5).

See also preferred embodiments on page 27 in Table 5, which disclose species teaching specific moieties. Note the exemplary compounds listed in the table such as 6-chloroindirubin-3'-oxime and 6-fluoroindirubin-3'-oxime (compounds 7d and 7b, respectively).

The Difference Between the Prior Art and the Claims (MPEP §2141.02)

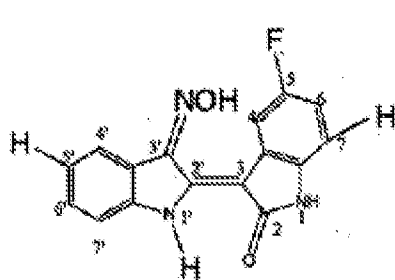
The difference between the prior art of *Lefoulon, et al.* and the instant invention is that there is homologous subject matter. Not all of the substituents are taught, however there is overlap between the substituents disclosed especially in view of the preferred embodiments taught by the prior art. The compounds in the instant application have the halogen located at the 5-position of the indirubin-3'-oxime core structure whereas the

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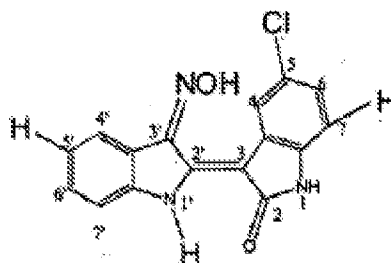
prior art teaches the indirubin-3'-oxime compound where the halogen is located at the 6-position.

Prima Facie Obviousness-The Rational and Motivation (MPEP §2142-2413)

Applicants are claiming compounds of the formula



and



wherein the fluorine or

chlorine atoms are located at the 5-position. The prior art reference of *Meijer, et al.* teaches a similar compound wherein the same compounds except the fluorine or chlorine atoms are located at the 6-position.

In In re Jones, 162 F.2d 638, 74 USPQ 152 (CCPA 1947), it was well established that compounds which differ only in the placement of substituents in a ring system is not patentable absent unexpected results. For example, it is obvious to prepare a 5-chloro or fluoro substituted indirubin-3'-oxime when the art teaches a 6-chloro or fluoror substituted indirubin-3'-oxime with a reasonable expectation of success. Specifically, placing halogen substitutents in different positions on a ring system of a well-known structure should give similar activities as the known compound and thus is obvious absent unexpected results. The prior art also teaches in table 5 on page 27 a variety of compounds including 6-chloroindirubin-3'-oxime and 5,6-dichloroindirubin-3'-oxime and the references further teaches that in previous studies it had been demonstrated that

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the indirubin derivatives substituted on position 5 exhibited an enhanced inhibitory activity (See paragraph 0213, page 21). Therefore, it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to prepare adjacent homologs based on the teachings of the preferred embodiments in the prior art. A strong prima facie obviousness has been established.

III. Conclusion

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 7:00 AM-3:30PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shawquia Young/

Examiner, Art Unit 1626

/Rebecca L Anderson/

Primary Examiner, Art Unit 1626